Inhibition of Apoptosis Overcomes Stage-Related Compatibility Barriers to Chimera Formation in Mouse Embryos.

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Public Summary:
Cell types more advanced in development than embryonic stem cells, such as EpiSCs, fail to contribute to chimeras when injected into pre-implantation-stage blastocysts, apparently because the injected cells undergo apoptosis. Here we show that transient promotion of cell survival through expression of the anti-apoptotic gene BCL2 enables EpiSCs and Sox17+ endoderm progenitors to integrate into blastocysts and contribute to chimeric embryos. Upon injection into blastocyst, BCL2-expressing EpiSCs contributed to all bodily tissues in chimeric animals while Sox17+ endoderm progenitors specifically contributed in a region-specific fashion to endodermal tissues. In addition, BCL2 expression enabled rat EpiSCs to contribute to mouse embryonic chimeras, thereby forming interspecies chimeras that could survive to adulthood. Our system therefore provides a method to overcome cellular compatibility issues that typically restrict chimera formation. Application of this type of approach could broaden the use of embryonic chimeras, including region-specific chimeras, for basic developmental biology research and regenerative medicine.

Scientific Abstract:
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